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Generation and Trapping of a Caged Cyclopentylidenecarbene

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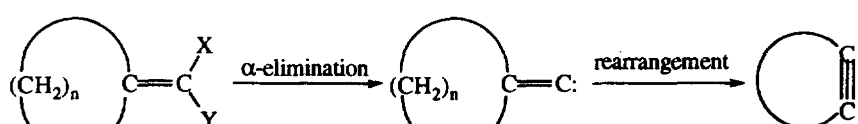
Abstract. The reactive intermediate that is produced both (i) via reaction of 8-(dibromomethylene)-pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**6**) with *n*-BuLi-THF and (ii) via the corresponding reaction of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8-one (**11**) with diethyl diazomethylphosphonate (DAMP) has been shown to be vinylidenecarbene **7a** rather than the corresponding cycloalkyne, **7b**.

Bromomethylene- and dibromomethylenecycloalkanes have been widely employed as precursors to novel unsaturated carbenes and cycloalkynes.[1] Interestingly, α–elimination of Br_2 from dibromomethylenecyclobutane (**1**, X = Y = Br, n =3) results exclusively in formation of cyclopentyne; the putative vinylidenecarbene intermediate, **2**, cannot be trapped. When the elimination reaction is performed in the presence of an alkene, [2 + 2] cycloaddition occurs with concomitant formation of a substituted cyclobutene.[1] However, the situation appears

Scheme 1



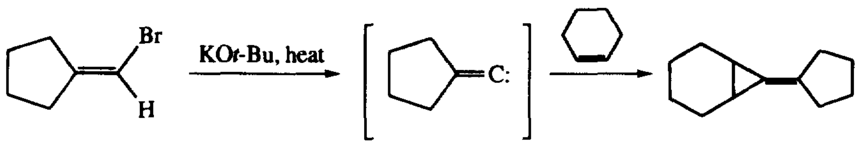
1: X = halogen, Y = H or halogen
n = 2-4, 6, 7, 9, 11

2: a vinylidenecarbene

3: a cycloalkyne

to be different for the case of **1** (n = 4). Thus, when bromomethylenecyclopentane (**4**) is heated with strong base in the presence of cyclohexene, cycloaddition of the corresponding intermediate vinylidenecarbene (**2**, n = 4) to the cyclohexene carbon-carbon double bond occurs, thereby affording **5** in low yield (Scheme 2).[2]

Scheme 2



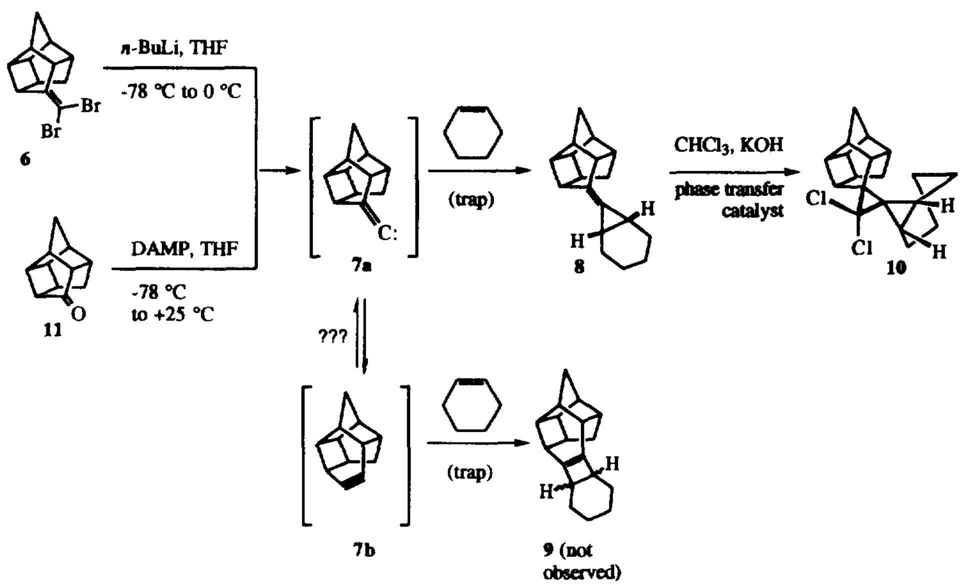
4

2 (n = 4)

5 (11%)[2]

Results and Discussion. In the present study, we have generated a reactive intermediate in two ways. First, the reaction of 8-(dibromomethylene)pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecane (**6**, Scheme 3) with *n*-BuLi-THF was performed at low temperature, and the reactive intermediate thereby produced was trapped *in situ* by cyclohexene. The resulting cycloadduct, **8**, subsequently was allowed to react with dichlorocarbene, and the structure of the resulting product, **10**, was established via application of X-ray crystallographic methods.[3] Similarly, the corresponding reaction of pentacyclo[5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$]undecan-8-one (**11**)[4] with diethyl diazomethylphosphonate (DAMP)[1c,5] produced **8** in 30% yield. These results suggest (i) that the same reactive intermediate was produced in both reactions and (ii) that this species is, in fact, vinylidenecarbene **7a** and not the corresponding cycloalkyne, **7b**.

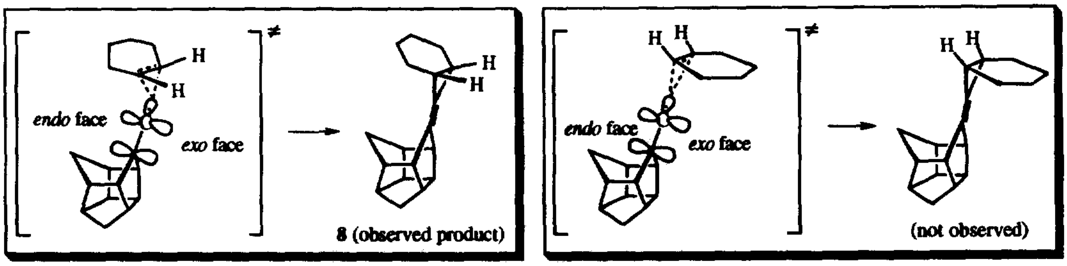
Scheme 3



It should be noted that vinylidenecarbene **7a** is unusual in that it contains diastereotopically differentiated π–faces. Of particular interest is the fact that cycloadduct **8** results via approach of cyclohexene upon the more highly sterically congested *endo* face of the π–system in **7a** (see Scheme 4). The fact that the major product, **8**, presumably formed via cycloaddition of vinylidenecarbene **7a** to the carbon-carbon double bond in cyclohexene, results via prefential approach of the cyclohexene ring upon the *endo* face of the carbene is somewhat surprising. The reasons for this observed stereopreference are not clear at present.

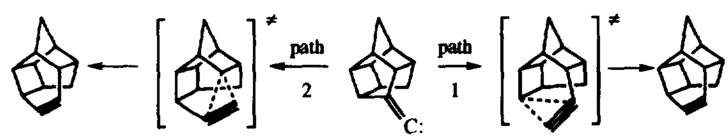
Results of Quantum Mechanical Calculations. We have performed semiempirical molecular orbital (AM1) and also ab initio calculations [HF/3-21(G*) and HF/6-31(G*)] for the rearrangement of vinylidenecarbene **7a** to the corresponding cyclohexyne (**7b**).[6] The results of the AM1 calculations indicate that vinylidenecarbene **7a** is preferred thermodynamically by 6.6 kcal-mol^{-1} *vis-à-vis* **7b** (see Table 1). Two transition states, **TS-1** and **TS-2** (Scheme 5) were also considered explicitly by using the AM1 Hamiltonian. It was found

Scheme 4



that the energy required to surmount **TS-2** is prohibitively high (Table 1); thus, **TS-1** was used in subsequent ab initio calculations (*vide infra*).

Scheme 5



7b | **TS-2** ($\Delta G^{\neq}$ = 88.8 kcal-mol^{-1} (AM1) | **7a** | **TS-1** ($\Delta G^{\neq}$ = 37.4 kcal-mol^{-1} (AM1) | **7b**

Table 1. Absolute and relative energies from semiempirical and ab initio calculations[a]

Computational Method	Vinylidenecarbene (**7a**)	Cycloalkyne (**7b**)	**TS-1**	**TS-2**
AM1 (kcal-mol^{-1})	147.38758 (0)	153.94512 (6.6)	184.84403 (37.4)	236.24720 (88.8)
HF/3-21(G*) (total energies, in hartrees)	-458.71852 (0)	-458.68723 (19.6)	-458.67003 (30.4)	
HF/6-31(G*)[b] (total energies, in hartrees)	-461.03539 (0)	-461.00537 (18.8)	-460.99899 (22.8)	

[a]Relative energies(kcal-mol^{-1}) for each series are in parentheses.

[b]The zero-point energy contribution has been applied to these values.

The results of the corresponding ab initio calculations also are presented in Table 1. It should be noted that the ab initio computational results indicate a much greater degree of instability for **7b** relative to **7a** than was suggested by the corresponding AM1 computational results. The results obtained at the highest level of approximation used in our study [i. e., HF/6-31(G*), with the zero point vibrational energy correction applied] indicate that the rearrangement of **7a** to **7b** via **TS-1** must traverse a kinetic barrier of 22.8 kcal-mol^{-1} and is accompanied by an enthalpic change of +18.8 kcal-mol^{-1}.

Interestingly, the experimental and computational results presented herein contrast with the corresponding results that have been reported for the cyclopentylidenecarbene-cyclohexyne equilibrium.[7] Thus, Johnson and Daoust[7b] have calculated a modest energy barrier of *ca.* 11-24 kcal-mol^{-1} for rearrangement of cyclopentylidenecarbene to cyclohexyne; the predicted enthalpy change for this process is -14 to -17 kcal-mol^{-1}. In contrast to this result, we find carbene **7a** to be preferred thermodynamically *vis-à-vis* the corresponding cycloalkyne (**7b**).

Summary and Conclusions. A reactive intermediate was generated by treating 8-(dibromomethylene)pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**6**, Scheme 3) with *n*-BuLi-THF at low temperature. This species, vinylidenecarbene **7a**, could be trapped *in situ* by cyclohexene, thereby affording the corresponding cycloadduct, **8**. The same species, **7a**, was produced via reaction of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8-one (**11**)[4] with DAMP.[1c,5] The results of semiempirical and ab initio calculations are consistent with our observation that vinylidenecarbene **7a** shows no tendency to rearrange to the corresponding cycloalkyne, **7b**, when generated under the conditions employed in this study. Additional calculations are underway in an effort to improve our understanding of the factors that contribute to the relative stabilities of **7a** and **7b**.

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References and Footnotes

1. (a) Fitjer, L.; Kliebisch, U.; Wehle, D.; Modaressi, S. *Tetrahedron Lett.* **1982**, *23*, 1661. (b) Gilbert, J. C.; Baze, M. E. *J. Am. Chem. Soc.* **1984**, *106*, 1885. (c) Gilbert, J. C.; Giamalva, D. H. *J. Org. Chem.* **1992**, *57*, 4185. (d) Gilbert, J. C.; Kirschner, S. *Tetrahedron Lett.* **1993**, *34*, 599, 603.

2. (a) Erickson, K. L.; Wolinsky, J. *J. Am. Chem. Soc.* **1965**, *87*, 1142. (b) Similarly, ultrasonicated reaction of dibromomethylenecyclopentane with Li in THF in the presence of cyclohexene has been reported to afford **5** in 67% yield. *See:* Xu, L.; Lin, G. Tao, F.; Brinker, U. H. *Acta Chem. Scand.* **1992**, *46*, 650. We thank a referee for calling this publication to our attention.

3. Selected X-ray crystallographic data for **10** ($C_{19}H_{22}Cl_2$): Space group: P-1 bar; a = 6.4549 (8) Å; b = 10.1281 (9) Å; c = 12.413 (1) Å; α = 72.695 (7)°; β = 88.467 (9) °; γ = 87.284 (9)°; V = 773.8 (1) Å^3; Z = 2; μ = 4.10 cm^{-1}; D_{calc} = 1.379 g-cm^{-3}; R = 0.0652; R_w = 0.0699. A complete description will be given in the full paper.

4. We have previously reported the synthesis of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8-one; see: Flippen-Anderson, J. L.; Gilardi, R.; George, C.; Marchand, A. P.; Jin, P.-W.; Deshpande, M. N. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1988**, *C44*, 1617.

5. We thank Professor John C. Gilbert, Department of Chemistry, University of Texas at Austin, for having provided a generous sample of DAMP for our use.

6. All calculations were performed by using SPARTAN software on an SGI INDIGO2 platform (UNIX operating system). Full geometry optimizations were performed at semiempirical (AM1) and ab initio [HF/3-21(G*) and HF/6-31(G*)] levels. Vibrational frequency calculations were used to characterize the first-order transition state (single imaginary frequency). SPARTAN computer software (version 4.0.3) was purchased from Wavefunction, Inc., 18401 von Karman, Suite 370, Irvine, CA 92715.

7. (a) Tseng, J.; McKee, M.; Shevlin, P. B. *J. Am. Chem. Soc.* **1987**, *109*, 5474. (b) Johnson, R. P.; Daoust, K. J. *J. Am. Chem.Soc.* **1995**, *117*, 362.

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